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Maternal experiences of childhood maltreatment moderate patterns of mother–infant cortisol regulation under stress

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Abstract

The relation between maternal and infant cortisol responses has been a subject of intense research over the past decade. Relatedly, it has been hypothesized that maternal history of childhood maltreatment (MCM) impacts stress regulation across generations. The current study employed four statistical approaches to determine how MCM influences the cortisol responses of 150 mothers and their 4-month-old infants during the Still-Face Paradigm. Results indicated that MCM moderated cortisol patterns in several ways. First, lower MCM mothers and infants had strong positive associations between cortisol levels measured at the same time point, whereas higher MCM mothers and infants did not show an association. Second, infants of higher MCM mothers had cortisol levels that were moderately high and remained elevated over the procedure, whereas infants of lower MCM mothers had decreasing cortisol levels over time. Third, higher MCM mothers and infants showed increasingly divergent cortisol levels over time, compared to lower MCM dyads. Finally, patterns of cross-lagged influence of infant cortisol on subsequent maternal cortisol were moderated by MCM, such that lower MCM mothers were influenced by their infants' cortisol levels at earlier time points than higher MCM mothers. These findings highlight MCM as one contributor to processes of stress regulation in the mother–infant dyad.

KEYWORDS
child maltreatment, cortisol, HPA Axis, mother-infant relations

1 | INTRODUCTION

The process of social exchange between mothers and infants occurs over multiple systems (hormonal, physiological, behavioral) is transactional and dynamic, and transpires over time (Cicchetti & Toth, 2009; Feldman, 2012). The construct of "attunement" has emerged as a central process through which mother and infant increasingly mirror or match one another in physiological state over time (e.g., Atkinson et al., 2016; Feldman, 2012; Fleming et al., 1999). Within this literature, multiple operationalizations and analytic approaches have been used to assess the mutual physiological influence between mothers and infants. Importantly, associations between maternal and infant physiology are known to be impacted by relational risk factors. While maternal history of childhood maltreatment (MCM) has been linked to disruptions to the mother–infant relationship (e.g., Alink et al., 2019), MCM has not been assessed thoroughly in relation to mother–infant cortisol regulation. Using a comprehensive statistical approach, the present study evaluates MCM as a potential moderator of relations between maternal and infant cortisol early in the first year of life.

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Maternal history of childhood maltreatment is a relational risk factor that can contribute to pernicious mental and physical health consequences across generations (e.g., Buss et al., 2017; Moog et al., 2018). MCM has been strongly associated with disrupted mother–infant relational experiences (e.g., Alink et al., 2019; Savage et al., 2019) and adverse child outcomes (e.g., Racine et al., 2018). Given the importance of quality of early care in the modulation of stress responses (Gunnar & Donzella, 2002), MCM may impact the development of infant stress physiology, which can have enduring implications for the child's stress response system over time (Feldman, 2012).

The literature on infant stress physiology has focused heavily on the hypothalamic–pituitary–adrenal (HPA) axis because the HPA axis is the primary biological stress response system in humans and is activated under acute stress, resulting in increased production of the hormone cortisol. Importantly, alterations in the functioning of maternal and infant HPA axes are hypothesized to contribute to the intergenerational effects of child maltreatment (Brand et al., 2010; Buss et al., 2017). However, MCM has rarely been examined in relation to maternal and infant cortisol levels over the course of an acute stressor. Two studies found that mothers with a history of child maltreatment, when assessed at infant age 6 months, displayed declining cortisol levels over the course of an acute infant stressor compared to mothers with lower history of maltreatment (Brand et al., 2010; Juul et al., 2016). Further, MCM was associated with lower infant baseline cortisol levels but was not related to change in infant cortisol levels over time (Brand et al., 2010). Importantly, research has yet to assess how MCM impacts the complex and dynamic relations between maternal and infant cortisol levels over time during an acute stress paradigm.

With the increasing sophistication of physiological attunement research, it has become more difficult to house the many facets of the relations between maternal and infant cortisol under the single construct of "attunement," as reviewed by Bernard et al. (2017). One early corollary of an attunement model was that adaptive physiological regulation was defined primarily in terms of a positive correlation between cortisol levels or cortisol trajectories of mothers and infants (Van Bakel & Riksen-Walraven, 2008; Middlemiss et al., 2012; Sethre-Hofstad et al., 2002). However, Nofech-Mozes et al. (2019) cautioned that positive/adaptive physiological regulation does not always mean similar physiology in the mother and infant. Rather, adaptive regulation depends on the ability of one partner to respond and adjust appropriately to the other, which may mean downregulating physiology in the face of high arousal in the other partner or vice versa. Nofech-Mozes et al. (2019) further point out that positive associations between maternal and infant cortisol could reflect maladaptive physiological regulation, in that highly aroused mothers may overstimulate their infants to high levels of arousal, whereas mothers with blunted arousal may understimulate their infants such that infant cortisol levels remain blunted. In addition, infant physiological state may have similar adaptive or maladaptive influences on maternal state.

Additionally, as Bernard et al. (2017) have cogently reviewed, the many current analytic methods used to characterize the relations between maternal and infant cortisol over time do not index a single process or construct. For example, some studies have focused on correlations between maternal and infant cortisol before and after induced stress (Middlemiss et al., 2012; Thompson & Trevathan, 2008). While the frequently observed positive associations are often interpreted to indicate that mothers influence their infants' cortisol levels, it is equally plausible that infants influence their mothers' cortisol levels. Other studies have examined associations between maternal and infant cortisol trajectories over the course of mild challenges. Laurent et al. (2012) used multilevel modeling (MLM) to show that maternal and infant cortisol trajectories were positively associated over the course of both a separation stressor and a clean-up task at 18 months. Similarly, Atkinson et al. (2013) demonstrated that mother and infant average cortisol levels and change in cortisol levels were positively associated during frustration and separation challenges at 16 and 17 months. Hibel et al. (2015) further showed that mother–infant cortisol trajectories were positively correlated in infancy and toddlerhood during the Lab-TAB (Goldsmith & Rothbart, 1988) stressors. Notably, these positive associations in cortisol trajectories were moderated by maternal and infant characteristics (Atkinson et al., 2013; Hibel et al., 2015; Laurent et al., 2012), suggesting another level of complexity in the associations between maternal and infant cortisol.

In order to assess more directly who influences whom during infant stress paradigms, Actor-Partner Influence Models (APIM) have been applied recently. Hendrix et al. (2018) found that, among mothers and their 6-month-old infants, the mothers' cortisol levels predicted their infants' cortisol levels at the subsequent time point, both in a separation paradigm and following a laboratory stress task. In addition, the infants' cortisol levels predicted their mothers' subsequent cortisol levels following the separation stressor. Bernard et al. (2017) found an influence from maternal cortisol to infant cortisol in a sample of 12-month-old infants who were subject to an arm restraint task. Finally, among mothers and their 17-month-old toddlers during a separation stressor, mothers' cortisol levels predicted toddlers' subsequent cortisol levels and vice versa, indicating mutual influence (Nofech-Mozes et al., 2019).

Investigators also have begun to examine how relations between maternal and infant cortisol vary under conditions of social risk, including maternal experiences of intimate partner violence (IPV; Bernard et al., 2017; Hibel et al., 2009), maternal depression (Laurent et al., 2011), disrupted maternal interaction (Crockett et al., 2013), and child attachment disorganization (Nofech-Mozes et al. 2019). One of the studies found stronger relations between maternal and infant cortisol under conditions of heightened social risk (Hibel et al., 2009), whereas the other three studies found weaker associations between maternal and infant cortisol under conditions of heightened social risk (Bernard et al., 2017; Crockett et al., 2013; Nofech-Mozes et al. 2019). Two of the above studies also quantified divergence in maternal and infant cortisol over time, as moderated by risk. Crockett et al. (2013) found that mother–infant dyads characterized by highly disrupted interaction demonstrated greater absolute differences in cortisol over the course of the stressor than

dyads with less disrupted interaction. Similarly, Nofech-Mozes et al. (2019) demonstrated that mother–infant dyads characterized by disorganized infant attachment had larger absolute differences between maternal and infant cortisol over the course of the stressor than mother–infant dyads characterized by organized attachment. Thus, maladaptive mother–infant relationship processes may be associated with greater divergence in maternal and infant cortisol levels over time.

Taken together, the research to date indicates that (a) different methods are needed to quantify different aspects of the relations between mother and infant cortisol, and (b) a number of relational risk factors may moderate these associations. To our knowledge, no study has examined MCM as a potential moderator of the relations between maternal and infant cortisol, including concurrent mother–infant correlations, mother–infant difference analysis, and cross-lagged assessments of mother–infant cortisol influence across time.

Analyses of maternal-infant influence, particularly in relation to HPA axis functioning, must consider infant age given that patterns of regulation and processes of influence may change over the first year of life (e.g., Gunnar & Donzella, 2002). Many studies on the relations between maternal and infant cortisol levels focus on infants 12 months or older (e.g., Atkinson et al., 2013; Laurent et al., 2012). Only one study included infants younger than 5 months of age (Crockett et al., 2013). This study used the Still-Face Paradigm (SFP) as a mild to moderate infant stressor (Tronick et al., 1978), based on a large literature validating the SFP in relation to evoking negative affect in infants (Mesman et al., 2009). Importantly, research has demonstrated that the SFP elicits a cortisol response in infants ranging from 2 to 8 months of age (Crockett et al., 2013; Erickson et al., 2013; Feldman et al., 2010; Grant et al., 2009; Haley & Stansbury, 2003; Lewis & Ramsay, 2005; Martinez-Torteya et al., 2014; Montirosso et al., 2013), albeit with considerable heterogeneity in responses. For example, in a sample of 7-month-old infants, Martinez-Torteya et al. (2014) found that 23% showed an increase from baseline to poststressor cortisol samples, 45% showed a decrease, and 22% showed an unstable pattern of cortisol change. The degree of infant cortisol reactivity to the SFP has been found to be moderated by maternal and relational factors, such as maternal mental health (Grant et al., 2009) and maternal caregiving behavior (Crockett et al., 2013; Grant et al., 2009; Martinez-Torteya et al., 2014). Research has not yet examined whether MCM is a moderator of mother–infant cortisol in response to the SFP.

1.1 | Aims of the current study

To thoroughly characterize relations between maternal and infant cortisol early in the first year of life and to determine how maternal MCM impacts these relations, we employed all of the primary analytic methods used in the literature, that is, (a) MLM of maternal and infant concurrent cortisol levels over the course of the stressor, (b) repeated measure modeling of change in mother and infant cortisol levels over time, (c) mother–infant difference analysis, and (d) cross-lagged MLM, to assess patterns of cortisol output in mothers and their 4-month-old infants in response to the SFP. We hypothesized that higher levels of MCM would be related to lower concurrent associations between maternal and infant cortisol, given the preponderance of evidence that risk is associated with increased mother–infant differences. We further hypothesized that, for both mothers and infants, patterns of cortisol response over time would be moderated by MCM. Third, given that prior work has found that social risk factors are associated with larger absolute differences between maternal and infant cortisol over the course of a stressor, we hypothesized that higher MCM would be associated with larger absolute mother–infant differences in repeated measures of cortisol levels. Lastly, prior studies in older infants have suggested a reciprocal influence of maternal and infant cortisol on one another. Thus, we hypothesized that reciprocal patterns of physiological influence in the dyad would occur, moderated by MCM.

2 | METHODS

2.1 | Participants

One hundred and fifty mother–infant pairs participated in the Mother-Infant Neurobiological Development (MIND) study, a study of mechanisms contributing to the intergenerational transmission of child maltreatment. Participants were recruited through prenatal classes, community flyers, and local birth records. Mothers were screened by phone using the Adverse Childhood Experiences questionnaire (Felitti et al., 1998), to ensure the sample was stratified such that half (51%) of the mothers had experienced childhood abuse (physical, emotional, and/or sexual), neglect, and/or exposure to domestic violence. Exclusion criteria were: (a) English not a primary language spoken at home, (b) maternal age over 44 years at time of infant birth, (c) infant born before 36 weeks gestation and/or weighing less than 2500 g at birth, and (d) infant had a congenital developmental disorder or birth defect. Mothers ranged in age from 18 to 40 years (M = 32.11, SD = 4.32). Infants (45% male) were approximately 4 months of age (M = 4.79 months, SD = 1.02 months) at the time of assessment. The sample was primarily White (72.5% mothers, 65.3% infants), with the remainder of the sample Black (9.4% mothers, 8.7% infants) and of other racial backgrounds (23.4% mothers, 26% infants). A range of annual family income was included, with 30.6% of the sample earning $50,000 or below, 28.6% earning $50,000–$100,000, and 40.8% earning $100,000 and above.

2.2 | Procedures

Assessments were conducted during a home visit to minimize the effects of travel and entry into a strange laboratory environment on cortisol levels. All visits were conducted between 12:00 and 18:00 h to minimize the effects of the circadian rhythm of cortisol. The

majority (87%) of study visits occurred between 12:00 and 14:00 h (63% between 12:00 and 14:00 h, 24% between 14:00 and 16:00 h); however, due to participant scheduling requests, 13% of the visits occurred between 16:00 and 18:00 h. Saliva collection time was negatively correlated with maternal cortisol levels (r range −.254 to −.289, $p < .05$), but not significantly correlated with infant cortisol levels (r range −.003 to .106, $p > .05$). Time of sampling was controlled in all analyses. Mothers and infants participated in a 10-min video-recorded SFP (Tronick et al., 1978), and mothers completed a comprehensive measure of their experiences of child maltreatment. Saliva was collected from mothers and infants at three time points to assess cortisol (details below).

2.3 | Measures

2.3.1 | Still-face paradigm

In a comfortable area of their home, mothers and infants were seated face-to-face to participate in the SFP (Tronick et al., 1978), which consists of three episodes. During the first episode, the mother was instructed to interact with her infant as she normally would for 3 min. Next, the mother displayed a neutral face and did not interact, touch, or vocalize to her infant for 2 min (still-face period, stressor). Finally, the mother engaged in a period of typical interaction for 5 min (reunion period, recovery). A meta-analysis has validated that the SFP serves as a mild to moderate social stressor for the infant, reducing positive affect and increasing negative affect (Mesman et al., 2009).

2.3.2 | Salivary cortisol

Following accepted procedures for capturing cortisol output over the course of an acute stressor (Dickerson & Kemeny, 2004), saliva was collected from mothers and infants at three time points. The three samples corresponded to the time points prior to initiation of the SFP (Baseline), 20 min after the still-face period ended (+20 min), and 40 min after the still-face period ended (+40 min). Mothers filled out questionnaires during the 55 min from the end of the second face-to-face interaction to the final saliva collection. On average, the baseline, post-20 min and post-40 min samples were taken at 13:58 h (SD = 1 h 38 min), 14:32 h (SD = 1 h 27 min), and 14:52 h (SD = 1 h 27 min), respectively. Mothers and infants did not eat or drink anything 30 min before the first saliva sample was taken to avoid saliva contamination. Sorbettes (Salimetrics, State College, PA) were used to collect maternal and infant saliva at each time point. Saliva samples were processed and assayed in the Kirschbaum laboratory at the Department of Psychology, Technical University of Dresden. Samples were centrifuged for 15 min and 3000 rpm. Samples were assayed in duplicate, and average values were used in analyses. Average inter- and intra-assay variability values were below 10%.

2.3.3 | Maternal history of childhood maltreatment

After completion of the SFP, mothers completed the 75-item Maltreatment and Abuse Chronology of Exposure scale (MACE; Teicher & Parigger, 2015). The MACE assesses the severity of 10 types of maltreatment in each year of childhood, as well as overall severity of child maltreatment through age 18 (Teicher & Parigger, 2015). Types of child maltreatment assessed included verbal abuse, nonverbal emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect, peer emotional abuse, peer physical bullying, witnessing interparental violence, and witnessing violence to siblings. The MACE total score correlates highly with other measures of child maltreatment, including the Childhood Trauma Questionnaire (CTQ) and the ACE questionnaire (Teicher & Parigger, 2015). The MACE also has high test–retest reliability (Teicher & Parigger, 2015). In the present study, the overall maltreatment severity score (possible scores ranging from 0 to 100), which takes into account all types of maltreatment across ages 0–18, was used as the index of MCM.

2.3.4 | Sociodemographics

Mothers self-reported their age, race, ethnicity, educational attainment, household income level, and the infant's race and ethnicity.

2.4 | Statistical analyses

2.4.1 | Analytic models

Prior to analyses, cortisol values were log-transformed and winsorized to correct for skewness and extreme values. Primary predictor variables (cortisol, maternal childhood maltreatment scores) were grand-mean centered. All multiple comparisons were Tukey-adjusted. Four analytic models were used to evaluate the research questions. In all analyses, mothers and infants were treated as distinguishable dyads. In all models, we treated each measurement of cortisol as a different condition, rather than treating time as a linear predictor. The rationale for not treating time as a linear predictor was that a social stressor occurred between the baseline and the later two measurements, creating an experimental manipulation and thus a different context for each cortisol measurement.

First, in order to evaluate concurrent associations between maternal and infant cortisol, we used a multi-level repeated measures model, using the nlme package in R. The first hypothesis addressed whether mother's history of child maltreatment would be associated with decreased concurrent relations between maternal and infant cortisol. We tested both whether mother's cortisol predicted infant cortisol concurrently and vice versa, as results may differ depending on which person's cortisol is the predictor and which is the outcome. This MLM included time as the lower level unit and dyad as the upper level unit. We used an autoregressive, lag one model for

the error structure of the random effects. Consistent with Bernard et al. (2017), this was done to allow for stability in cortisol over repeated measures. For both models, we added only parameters that improved model fit, testing whether a random effect for dyad and repeated measure improved the model (allowing individual trajectories of cortisol over time).

Second, to examine mean levels of maternal and infant cortisol over time and to assess whether MCM predicted differences in cortisol levels across measurement points, a dyadic repeated measures model was estimated using generalized least squares (gls) in R, with MCM as a moderator. We used a two-intercept model to estimate the separate intercepts for infants and mothers.

Third, consistent with previous research (Crockett et al., 2013; Nofech-Mozes et al., 2019), we evaluated whether absolute differences in mean cortisol levels between mothers and infants varied across measurement points. We used the same approach as Nofech-Mozes et al. (2019), in which a difference score was calculated by subtracting maternal cortisol from infant cortisol, then adding the absolute value of the lowest difference score for each time point. This method preserves the rank order among dyadic difference scores. We used MLM to account for dependencies in cortisol levels within dyads. Using a two-level model, we again treated measurement point as a repeated measure, with MCM as a level 2 predictor. We iteratively built the model beginning with a null model, proceeding according to a priori decisions and using log-likelihood ratio tests to evaluate model fit. We tested random effects, assessing between-dyad variation in intercepts and allowing the effect of MCM to vary between dyads.

Fourth, we estimated a stability-influence (cross-lagged) multilevel model (e.g., Thorson et al., 2018), using the nlme package in R (R Core Team, 2013). In actor-partner stability-influence models (APIM), actor effects refer to the stability in the measure within the person over time, whereas partner effects refer to influence of one partner on the other over time. Thus, we assessed whether a mother's cortisol at one measurement point was predicted both by her own previous cortisol level (actor effect) and by her infant's previous cortisol level (partner effect). Infants' cortisol levels were likewise predicted by both their own previous cortisol levels (actor effect) and by their mothers' previous cortisol levels (partner effect).

2.4.2 | Missing data

Missing data for cortisol were as follows: 6.0% for mother baseline, +20, and +40 min, and 7.9%, 10.6%, and 9.3% for infant baseline, +20, and +40 min, respectively. The analytic models used here accommodate missing data, so all available data were used. Participants were only excluded from analyses if they were missing all three cortisol time points (N = 8.5%). Missing infant cortisol values were primarily due to insufficient saliva collected because of infant fussiness when sampling saliva. Missing maternal cortisol was due to insufficient saliva (possibly due to dry mouth). No MACE data were missing.

TABLE 1 Descriptive statistics for maternal and infant cortisol values.

	M	*SD*	Range
Infant baseline cortisol	1.176	0.154	1.02–1.71
Infant +20 cortisol	1.143	0.142	1.02–2.15
Infant +40 cortisol	1.146	0.161	1.02–1.75
Mother baseline cortisol	1.106	0.068	1.01–1.37
Mother +20 cortisol	1.087	0.060	1.01–1.31
Mother +40 cortisol	1.078	0.051	1.01–1.29

Cortisol values are log-transformed and winsorized. +20 cortisol = 20 min after cessation of the still-face episode of the Still-Face Paradigm. +40 cortisol = 40 min after cessation of the still-face episode of the Still-Face Paradigm.

3 | RESULTS

3.1 | Descriptive statistics and preliminary analyses

MACE overall severity scores, which were used in the analyses, ranged from 0 to 75 (M = 18.49, SD = 17.48).[1] The means, standard deviations, and ranges of maternal and infant cortisol values are reported in Table 1. MACE scores were not significantly correlated with either maternal or infant cortisol levels at any time point (Table 2).

In accordance with previous research (e.g., Dickerson & Kemeny, 2004), time of day of cortisol sampling was included as a covariate in all analyses. We also initially controlled for maternal and infant race/ethnicity, infant age and gender, and household income. None of these variables were found to contribute significantly to the models. Thus, for the sake of parsimony, we removed them from the models, which had no effect on the pattern of results.

3.2 | Associations between overall maternal and infant cortisol by MCM severity

As shown in bivariate correlations in Table 2, overall maternal and infant cortisol values were highly correlated. To assess our first hypothesis that concurrent levels of maternal and infant cortisol across the three time points would be positively associated, MLM models were run to assess the concurrent effect of maternal cortisol on infant cortisol and vice versa, as well as to assess whether any obtained effects were moderated by MCM. In the first MLM model, using maternal cortisol to predict infant cortisol, the main effects for maternal cortisol (b = .30, SE = 0.13, p < .05) and MCM (b = .17, .08, p < .05), and for their interaction (b = −.16, SE = 0.07, p < .05) were all significant. Simple slopes estimating the effect of maternal cortisol on infant cortisol at 1 SD above and below the mean for MCM showed a strong positive association between maternal and infant

TABLE 2 Correlations among main study variables.

	1	2	3	4	5	6
1. MACE	–					
2. Infant baseline cortisol	−0.118	–				
3. Infant +20 cortisol	-0.025	0.540**	–			
4. Infant +40 cortisol	0.103	0.597**	0.791**	–		
5. Mother baseline cortisol	0.035	0.275**	0.266**	0.336**	–	
6. Mother +20 cortisol	−0.075	0.392**	0.372**	0.342**	0.799**	–
7. Mother +40 cortisol	−0.089	0.309**	0.336**	0.270**	0.758**	0.842**

Cortisol values are log-transformed and winsorized. MACE = Maltreatment and Abuse Chronology of Exposure scale severity score. +20 cortisol = 20 min after cessation of the still-face episode of the Still-Face Paradigm. +40 cortisol = 40 min after cessation of the still-face episode of the Still-Face Paradigm.

**$p < .01$.

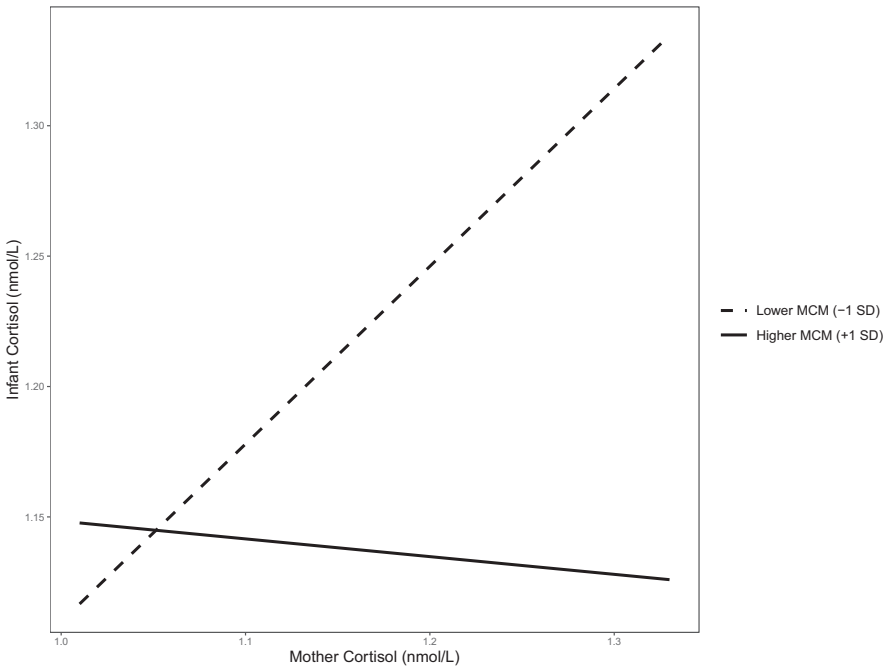

FIGURE 1 Concurrent associations between maternal and infant cortisol as a function of maternal childhood maltreatment (MCM). Note. Cortisol values are log-transformed (nmol/L) and winsorized. MACE scores of 1 standard deviation below (−1SD) and 1 standard deviation above (+1SD) the mean were chosen to depict lower childhood maltreatment and higher childhood maltreatment. Among lower MCM dyads, maternal cortisol is positively associated with infant cortisol levels. In contrast, among higher MCM dyads, maternal cortisol is not associated with infant cortisol levels.

cortisol for low MCM dyads ($b = .70$, $SE = 0.19$, $p < .001$). There was no association between maternal and infant cortisol for high MCM dyads ($b = -.09$, $SE = 0.24$, $p = .726$). A graph of this interaction is shown in Figure 1. In the second model, we found that infant cortisol did not significantly predict maternal cortisol, reaching only trend level ($p = .073$). When including MCM as a moderator, neither the main effect for MCM nor the interaction with child cortisol were significant.

3.3 | Changes in cortisol over the course of the stressor for mother and infant by MCM severity

While the first analysis assessed overall associations between maternal and infant cortisol levels, the second model assessed changes in maternal and infant cortisol levels over the three measurement points and whether any changes in cortisol were moderated by severity of MCM. To predict cortisol from person (mother or infant), measurement point (baseline, +20, +40 min), MCM severity (continuous variable), and all possible two-way and three-way interactions, we first fit a repeated-measures dyadic model using the gls function from the nlme package in R. A generalized least squares (GLS) model was used to allow for different variances for person and condition and for all covariances (between mothers and infants by condition) to be estimated.

Significant main effects were qualified by two-way and three-way interactions. We report the main effects only to describe the overall trends in the data. The main effect for person ($b = .03$, $SE = 0.005$, $p < .001$) indicated that, on average, mothers had lower cortisol values over the task compared to infants (see Table 2), consistent with previous literature (e.g., Hibel et al., 2009; Laurent et al., 2011). The main effect for measurement point ($b = -.01$, $SE = 0.003$,

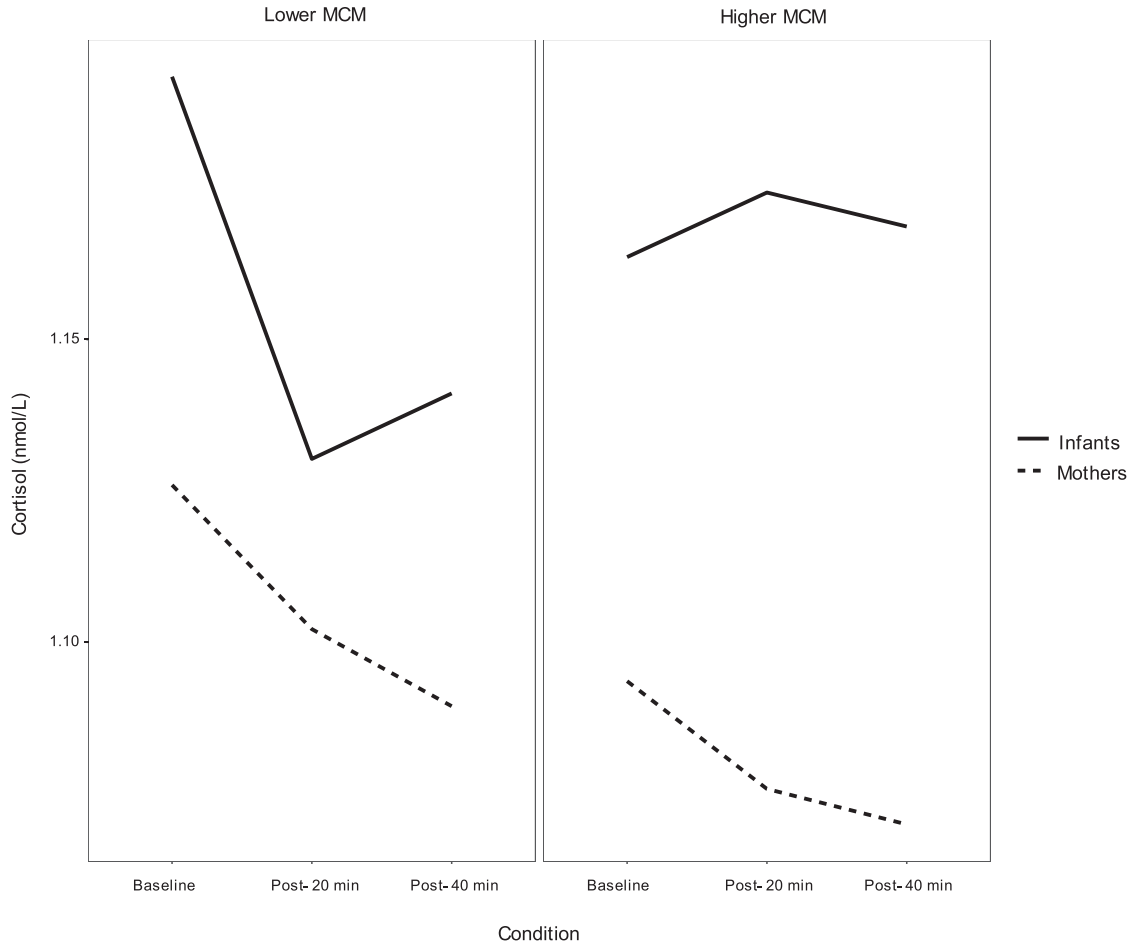

FIGURE 2 Maternal and infant cortisol by severity of mothers' childhood maltreatment: Dyadic repeated measures. Note. Cortisol values are log-transformed (nmol/L) and winsorized. MACE scores of 1 standard deviation below (−1SD) and 1 standard deviation above (+1SD) the mean were chosen to depict lower maternal childhood maltreatment (MCM) and higher MCM.

$p < .001$) indicated that, across persons, cortisol measured 20 min after the SFP ($b = -.03$, $SE = 0.01$, $p < .005$) and 40 min after the SFP ($b = -.03$, $SE = 0.01$, $p < .01$) were both lower compared to baseline cortisol levels.

These main effects were qualified by a two-way interaction between measurement point and MCM severity ($b = .0003$, $SE = 0.0001$, $p < .01$) and a three-way interaction among person, measurement point, and MCM severity ($b = -.0004$, $SE = 0.0002$, $p < .05$). In the presence of the significant three-way interaction, the two-way interaction was not interpreted. The three-way interaction is graphed in Figure 2. The interaction reveals that, among mothers with lower MCM, infants had relatively higher cortisol levels at baseline, which decreased compared to baseline at the post 20-min ($b = .065$, $SE = 0.016$, $p < .001$) and post 40-min measurement points ($b = .056$, $SE = 0.017$, $p < .005$). In contrast, among mothers with higher MCM, infant baseline cortisol levels were lower compared to infants of lower MCM mothers ($b = .057$, $SE = 0.026$, $p < .05$), and infants of higher MCM mothers had cortisol levels that were stable over time, with mean cortisol levels that did not significantly decline from baseline to post 20-min ($b = .015$, $SE = 0.008$, $p = .160$) and post 40-min ($b = .013$, $SE = 0.009$, $p = .300$). Mothers' cortisol levels did not show a significant interaction effect. Both at higher MCM and lower MCM, mothers' cortisol levels decreased over time compared to baseline (baseline to post 20-min: $b = .019$, $SE = 0.004$, $p < .001$; post 20-min to post 40-min: $b = .010$, $SE = 0.003$, $p < .001$) (Figure 2).

3.4 | Differences between maternal and infant cortisol over time

Given prior findings relating risk status to increased absolute differences in maternal and infant cortisol levels over time (Crockett et al., 2013; Nofech-Mozes et al. 2019), we examined the effects of MCM and measurement point on mother–infant cortisol difference scores. This analysis allowed the quantification and significance testing of the divergence between maternal and infant cortisol levels over the course of the procedure (Figure 2). Model fit was assessed by comparing AIC values (lower values indicate better fit) and conducting log-likelihood ratio test comparisons during model building.[2]

The final model, which was based on a priori hypotheses, included measurement point, MCM severity, and the interaction between MCM severity and measurement point, as well as random

intercepts and a random effect for measurement point. We estimated the final model using maximum likelihood and compared it to the null model, $\chi^2(1) = 154.0$, $p < .001$. The main effect for MCM was not significant. However, there was an interaction between MCM and measurement point. Relative to baseline, MCM had a significant effect on mother–infant cortisol difference scores at post 20-min ($b = -.002$, $SE = 0.0001$, $p < .005$) and at post 40-min ($b = -.002$, $SE = 0.00001$, $p < .05$). The interaction indicated that lower MCM dyads exhibited decreased differences between mother and infant cortisol over later measurement points relative to baseline, whereas higher MCM dyads exhibited increased differences between maternal and infant cortisol at later measurement points relative to baseline (Figure 3).

3.5 | Cross-lagged models of influence between maternal and infant cortisol levels

Finally, we conducted an APIM to assess cross-lagged associations between maternal cortisol and infant cortisol across measurement points. This analytic method allows testing of effects of one person's cortisol level at one measurement point on the other person's level at the next measurement point.

A two-intercept model was used to estimate the separate intercepts and effects for both mothers and infants.[3] Regarding main effects before considering moderation by MCM severity and measurement point, the stability-influence model showed significant overall stability (actor) coefficients over measurement points for both mother ($b = .63$, $SE = 0.05$, $p < .001$) and infant ($b = .33$, $SE = 0.08$, $p < .001$). The stability findings indicate that mothers' and infants' own cortisol levels positively predicted their later cortisol levels. In contrast, again before considering effects of moderators, overall partner influence effects were significant from infants to mothers ($b = .08$, $SE = 0.02$, $p < .005$) but not from mothers to infants ($b = .17$, $SE = 0.17$, $p = .545$). This indicates that, overall, before considering moderator effects, mothers' cortisol levels were influenced by their infants' cortisol levels over the course of the task, but infants' cortisol levels were not influenced by their mothers' cortisol levels.

However, these actor and partner main effects were moderated by both measurement point and MCM. Regarding measurement point as moderator, infants showed increasing stability over time (Actor Cortisol * Measurement Point, $b = .24$, $SE = 0.09$, $p < .01$), with greater association between cortisol levels post 20-min to post 40-min than between cortisol levels at baseline and post 20-min. Regarding MCM severity as moderator, MCM moderated infant stability coefficients over time (Actor Cortisol*MCM, $b = .01$, $SE = 0.004$, $p < .01$), with infants of higher MCM mothers showing greater stability over time than infants of lower MCM mothers. This finding complements and reiterates the greater change effects over time among infants of lower MCM mothers observed using MLM above.

Regarding influence effects of one partner's cortisol on the other's cortisol, a three-way interaction emerged in mothers among partner (infant) cortisol, MCM, and measurement point ($b = -.006$, $SE = 0.001$, $p < .001$), indicating that infants' cortisol levels influenced mothers' cortisol levels as a function of both MCM and measurement point. There were no significant influences of maternal cortisol levels on infant cortisol levels. To aid in interpreting the three-way interaction on mother's cortisol levels, we reran the model excluding the nonsignificant effects of mother cortisol on infant cortisol and graphed the three-way interaction (Figure 4). As shown in Figure 4, the baseline cortisol levels of infants whose mothers had lower MCM (Figure 4 left panel, dotted line) *positively*

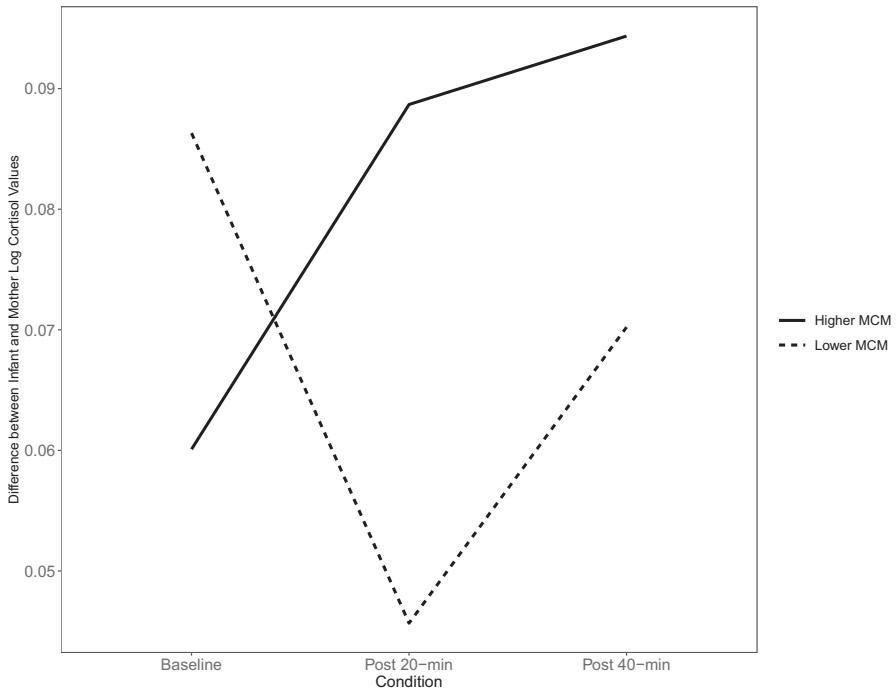

FIGURE 3 Differences between maternal and infant log cortisol values as a function of maternal childhood maltreatment (MCM). Note. Cortisol values are log-transformed (nmol/L) and winsorized. MACE scores of 1 standard deviation below (−1SD) and 1 standard deviation above (+1SD) the mean were chosen to depict lower MCM and higher MCM. Higher X-axis values reflect greater difference between infant and maternal cortisol levels at a given time point.

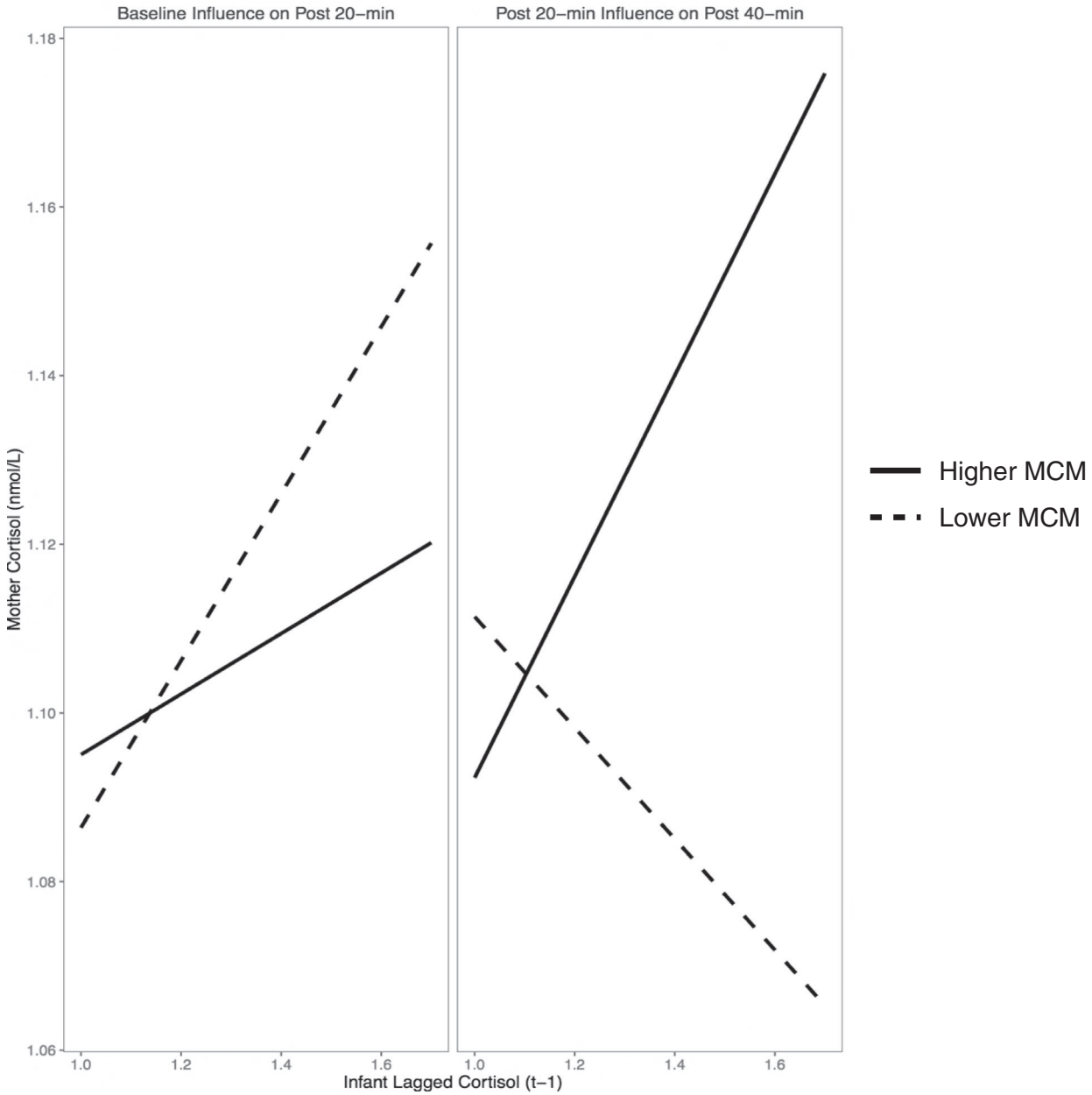

FIGURE 4 Infant cortisol influence on maternal cortisol as a function of time and maternal childhood maltreatment (MCM). Note. Cortisol values are log-transformed (nmol/L) and winsorized. MACE scores of 1 standard deviation below (−1SD) and 1 standard deviation above (+1SD) the mean were chosen to depict lower MCM and higher MCM. Effects refer to infant cortisol values at one measurement point predicting maternal cortisol values at the next measurement point. Among lower MCM dyads, infant's baseline cortisol levels positively influenced mothers' cortisol levels at post 20-min measurement, while infants' post 20-min cortisol levels negatively influenced their mothers' post 40-min cortisol levels. In contrast, among higher MCM dyads, infants' baseline cortisol levels did not influence mothers' post 20-min levels, but infants' post 20-min levels positively influenced their mothers' post 40-min cortisol levels.

influenced their mothers' post 20-min cortisol levels, while the post 20-min cortisol levels of the same infants *negatively* influenced their mothers' post 40-min cortisol levels (Figure 4 right panel, dotted line). In contrast, the cortisol levels of infants whose mothers had higher MCM did not significantly influence their mothers' cortisol levels from baseline to post 20-min (Figure 4 left panel, solid line). However, higher MCM infants' cortisol levels at post 20-min *positively* influenced their mothers' cortisol levels at post 40-min (Figure 4 right panel, solid line).

4 | DISCUSSION

Understanding how mother–infant cortisol regulation is influenced by the mother's experiences of child maltreatment is an important current scientific priority (Buss et al., 2017). The overarching aim of this study was to characterize maternal and infant cortisol responses to the mildly stressful SFP at 4 months of age and to assess how MCM might moderate their patterns of association. Specifically, we aimed to assess whether MCM moderated four types of relations

between maternal and infant cortisol: (a) concurrent associations between mother and infant cortisol levels over the course of the stressor; (b) repeated measures of the changes in maternal and infant cortisol levels over the course of the procedure (baseline, 20-min post stressor, 40-min post stressor); (c) absolute differences between the levels of maternal and infant cortisol over the course of the procedure; and (d) cross-lagged patterns of influence between maternal and infant cortisol over the course of the procedure.

In regard to our first hypothesis, MCM moderated the association between maternal and infant cortisol, such that only mothers with lower MCM and their infants, and not mothers with higher MCM and their infants, showed a significant positive association in their concurrent cortisol levels. This effect of MCM is consistent with recent studies that have shown less attunement in mother–infant cortisol levels in less optimal environments (e.g., Bernard et al., 2017). This finding extends previous reports of concurrent associations between maternal and infant cortisol in low-risk samples (Atkinson et al., 2013; Laurent et al., 2012; Middlemiss et al., 2012) by showing that these positive concurrent associations occur primarily in the context of lower MCM. This finding also extends prior work to include the directionality of this effect from mother to infant and not from infant to mother. Such early directionality from mother to infant is consistent with several mechanisms , including processes of behavioral regulation, shared genetics, and/or gestational effects on infant cortisol levels.

With respect to our second hypothesis, MCM moderated infants' cortisol levels over the course of the procedure. Infants of higher MCM mothers had lower baseline cortisol levels and less decline in cortisol over time compared to the baseline levels and trajectories of infants of lower MCM mothers. In the only other study relating MCM to infant cortisol reactivity to stress, Brand et al. (2010) also found that MCM was associated with lower baseline cortisol levels among 6-month-old infants. Regarding decline in cortisol over a stressor procedure, Atkinson et al. (2013) found that 16-month-olds of less sensitive mothers exhibited less pronounced decline in cortisol during a frustration-based stressor, compared to infants of more sensitive mothers. Thus, the current study adds to prior research by suggesting that MCM is associated with both lower infant baseline and higher and flatter infant cortisol levels following a stressor as early as 4 months of age.

In relation to the third hypothesis, MCM moderated the pattern of absolute differences between maternal and infant cortisol levels over measurement points. Dyads with higher MCM exhibited a pattern of increasing differences between maternal and infant cortisol over measurement points, whereas dyads with lower MCM exhibited a pattern of decreasing differences in cortisol levels from baseline. Notably, two prior studies have shown similar patterns of findings. Among mothers and their 16-month-olds, Nofech-Mozes et al. (2019) found that, compared to dyads with organized infants, dyads with disorganized infants showed greater mother–infant differences in cortisol levels over the course of a stressor, with infants exhibiting increasing cortisol and mothers exhibiting decreasing cortisol. Similarly, Crockett et al. (2013), using the SFP at 4 months of age, found that mothers who were severely disrupted in interaction with their infants maintained very low cortisol levels across the SFP, while their infants' cortisol levels rose significantly (Crockett et al., 2013). Taken together, these findings underscore the value of absolute differences in cortisol levels as a risk-related index of dyadic physiologic dysregulation.

Finally, in relation to our fourth hypothesis, MCM was found to moderate the process of influence between maternal and infant cortisol levels. Mothers with lower MCM were influenced by their infants' cortisol levels from the outset of the procedure, whereas mothers with higher MCM were not influenced until after the still-face period. Specifically, infants of lower MCM mothers had baseline cortisol levels that were positively related to their mother's post 20-min cortisol levels, suggesting that mothers were responding in kind to the high baseline cortisol levels of their infants (Figure 2). Also, among dyads with lower MCM, infants' post 20-min cortisol levels were *negatively* related to their mothers' post 40-min cortisol levels. Thus, in the post still-face portion of the procedure, mothers with lower MCM appeared to be *countering* their infants' cortisol levels by upregulating or downregulating their own cortisol levels. This may imply that, if the infant disengages during the still-face, following the still-face period, the mother with lower MCM may experience increases in cortisol as she attempts to reengage the infant. Alternately, infants with a higher cortisol response to the still-face period may elicit a compensatory lowering of mother's cortisol to counter the normative negative infant affect in reaction to the still-face portion (Mesman et al., 2009). Coupling cortisol data with behavioral observation will be an important future direction for this research.

A different pattern of influence occurred among infants of mothers with higher levels of maltreatment. First, infants' cortisol levels at baseline had no significant influence on the mothers' cortisol levels at the post-20 min assessment. Thus, the cortisol levels of infants with higher MCM at the onset of the SFP did not seem to influence their mothers' cortisol levels. Possibly, mothers with higher MCM found attending to their infants' state while interacting with study personnel in the early phases of the protocol study more challenging. Contrary to the pattern seen among dyads with lower MCM, among dyads with higher MCM, influence from infant to mother occurred only after the still-face portion of the procedure. Thus, among dyads with higher MCM, infant cortisol increases after the stressor reliably led to maternal increases in cortisol, or conversely, infant decreases in cortisol were mirrored by maternal decreases in cortisol. This contrasts with the pattern of influence among dyads with lower MCM, where the infants' cortisol level to the still-face stressor period reliably led to a compensatory response by the mothers.

Taken together, the findings from our comprehensive analytic approach suggest that concurrent associations, difference scores, and cortisol change and influence over time should be considered jointly to understand the complex nature of mother–infant physiological attunement. Consideration of both mean cortisol levels and divergence in mother and infant cortisol levels over time contextualize the cortisol influence findings. The positive influence of infant

cortisol on maternal cortisol from baseline to post 20-min, as seen in dyads with lower MCM, was accompanied by a decrease in infant cortisol over time. In contrast, in dyads with higher MCM, there was no influence between infant and mother cortisol at the outset of the procedure, and the positive influence of infant cortisol on maternal cortisol from post 20-min to post 40-min was accompanied by continued elevation in infant cortisol over time. This pattern among dyads with higher MCM is further characterized by the lack of associations between mothers and infants in concurrent cortisol levels and by the increasing divergence in mother–infant cortisol levels over time. Overall, these findings indicate that in the context of relational risk, such as MCM, no single analytic approach provides a complete understanding of the relations between mother and infant physiology. Thus, a comprehensive analytic approach which examines both concurrent and cross-lagged associations is needed.

Contrary to our hypotheses, we did not find that maternal cortisol influenced infant cortisol over the course of the procedure. This finding differs from prior studies that assessed patterns of cortisol influence among mothers and older infants. Hendrix et al. (2018) found evidence for both infant influence on the mother and maternal influence on the infant at age 6 months. Bernard et al. (2017) found an influence only from maternal cortisol to infant cortisol at age 12 months. Finally, Nofech-Mozes et al. (2019) found a bidirectional influence of maternal and toddler cortisol levels. In contrast, in our sample of 4-month-old infants, only an influence of infant cortisol on subsequent maternal cortisol was confirmed. Notably, all prior studies involved infants older than 4 months. Given that establishing patterns of physiological and emotional regulation is a primary developmental task of the first year of life (Cassidy, 1994; Kopp, 1989; Scharfe, 2000), it is possible that processes of infant–mother influence change over this early period. Specifically, it is possible that early in the first year, the influence process is more heavily from infant to mother, as the mother follows and sensitively responds to the infant's cues. However, by the end of the first year, the mother may be more familiar with her infant's cues and more adept at anticipating her infant's states and regulating them more proactively. Additionally, as infants' developmental capacities expand, they become more active and intentional partners in dyadic interactions. More longitudinal research studies are needed to assess whether and how the direction of influence may change with age.

The present study provides novel evidence of the impact of MCM on the pattern of influence between maternal and infant cortisol levels at 4 months of age. However, the mechanisms that account for this impact are not established. Maternal behavior, particularly maternal sensitivity, is one factor that increases the positive associations between maternal and infant cortisol levels (e.g., Atkinson et al., 2013, 2016; Hibel et al., 2015). The basic tenet of this prior research is that cortisol is primarily regulated in relational contexts (e.g., Gunnar & Donzella, 2002; Hostinar & Gunnar, 2013; Timmons et al., 2015) and that the positive quality of the parent–child relationship influences the degree of association between maternal and infant cortisol (i.e., "attunement"). In addition, Buss et al. (2017) have suggested that cortisol dysregulation as a result of preexisting maternal stressors, such as MCM, may have its origins in the prenatal period, through epigenetic processes that alter expression of genes in stress-sensitive brain regions. Longitudinal studies are needed to better characterize both prenatal and postnatal contributions of MCM to infant cortisol regulation.

The findings of this study must be considered in the context of the study's limitations. First, mothers and infants participated in a single challenge, the SFP, at 4 months infant age. The HPA axis is rapidly developing and is responsive to relational regulation over the course of the first year (e.g., Gunnar & Donzella, 2002). Thus, longitudinal studies are needed that assess how MCM impacts mother–infant physiological influence over a range of infant ages and in diverse stressful contexts. Second, research is needed to understand how maternal and infant behavior, as well as other individual and contextual factors, such as genetics, maternal gestational stress, and current psychopathology, may mediate or moderate the impact of MCM on mother–infant cortisol. These factors were not included in the current study. Third, this study did not collect information on maternal sleep/wake time or breastfeeding status, both factors that have the potential to influence cortisol reactivity (Neelon et al., 2015; Wright et al., 2007). Fourth, this study focused solely on salivary cortisol reactivity to challenge. It will be important to assess whether MCM has a similar impact on mother–child physiological influence using other measures of HPA axis activity, including hair cortisol and diurnal salivary cortisol (e.g., Fuchs et al., 2016, 2017).

In summary, the current study found that maternal experiences of childhood maltreatment moderated several aspects of infant-mother cortisol responses during a mild stress procedure. The extant literature indicates that children of mothers who have experienced childhood maltreatment show a range of deleterious outcomes, including alterations in brain volume at birth (Moog et al., 2018), self-regulation difficulties (Delker et al., 2014; Haskett et al., 2012), and elevated rates of developmental psychopathology (e.g., Plant et al., 2018). Dysregulation in the infant stress response system may be one key mechanism in the intergenerational transmission of the effects of MCM (Buss et al., 2017; Moog et al., 2018). Thus, further understanding of how MCM affects the infant stress system is an important public health priority. The current report extends the literature by documenting a number of effects of MCM on mother–infant cortisol regulation as early as 4 months of age. These results have important implications for the early identification of infants at risk, so that supports can be implemented to prevent intergenerational effects of MCM.

DATA SHARING

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONFLICTS OF INTEREST

The authors of this manuscript do not have any conflict of interest to declare.

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ENDNOTES

[1] Types of maltreatment endorsed above the MACE cut scores were as follows: verbal abuse, 50.3%; nonverbal emotional abuse, 28.2%; physical abuse, 43.0%; sexual abuse, 28.2%; emotional neglect, 50.7%; physical neglect, 23.5%; witnessing interparental violence, 30.2%; witnessing violence to siblings, 16.1%; peer emotional abuse, 55.0%; and peer physical bullying, 31.1%.

[2] When only measurement point was included in the model (i.e., MCM was not in the model), fixed effects for measurement significantly improved model fit. Post hoc tests revealed that differences between maternal and infant cortisol levels did not change significantly when comparing baseline to post 20-min (p =.081), but differences were significantly greater both when comparing post 20-min to post 40-min (p <.001) and when comparing baseline to post 40-min (p <.001). Entering measurement as a random effect also significantly improved the model and showed that within person intercepts were negatively correlated with cortisol levels at the subsequent measurements.

[3] We considered a number of models to evaluate model fit. We found that a model with random intercepts for mother and infant (dummy coded) fit better than a base model (likelihood ratio =299.91, p <.001). An autoregressive correlation structure was evaluated, but fit indices were identical to a model with a correlated compound symmetry correlation structure that used fewer degrees of freedom. As potential moderators of lagged actor and partner cortisol levels, the final model included both MCM and measurement point (baseline, +20, +40 minutes).

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